ATTACHMENTS

Provided herewith is a replacement sequence listing consistent with the sequences provided in the specification as filed to add sequence ID numbers for sequences 30 and 31.

Prior art references are also provided in support of the adequacy of the specification and enablement of the pending claims.

VERIFICATION STATEMENT

I hereby state that the content of the paper copy of the Sequence Listing and the enclosed computer readable copy of the Sequence Listing are the same.

REMARKS

Applicant notes with appreciation the thoroughness of the examination embodied in the Paper 20070812 and the opportunity to distinguish the pending claims over the prior art of record. By way of this amendment, claims 1, 2, 7, 11 and 41 have been amended; claims 3, 5, 6, 9-10, 12-40 and 42 have been canceled in compliance with 37 CFR 1.144; and sequence listings for "MGAQ" and "MAIS" are submitted concurrently herewith in compliance with 37 CFR 1.821(a)/(d). Support for the amendment is found in the claims as filed and in the specification, particularly at lines 8-10 on page 18 of the specification.

Currently, claims 1, 2, 4, 7, 8, 11 and 41 are pending in the application.

Claims 1-2, 7-8, 11 and 41 stand rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. Claims 1-2, 7-8, 11 and 41 stand rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. Claims 7-8, 11 and 41 stand rejected under 35 U.S.C. §112, second paragraph, as being

indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Remarks Directed to Rejection of Claims 1-2, 7-8, 11 and 41 under 35 U.S.C. §112, First Paragraph, Written Description

The written description rejection has been maintained on the basis that the prior art teachings previously made of record by Applicant predating the effective filing date of the instant application were deemed inadequate in providing description of Hpr gene or protein other than human Hpr (Paper No. 20070812, page 6, first full sentence).

In response, the previously referenced Lugli et al. reference is bolstered by the attached references of McEvoy et al., Erickson et al., Shuey et al., Heidenreich et al. and Martinez et al. In particular, McEvoy et al. seems to have been referred to by Lugli et al. on the very point that a full length Hpr is present in a very limited number of species. With the concurrent submission of the above mentioned prior art references, Applicant reinstates the previous argument of record which is reproduced as below.

> Further, Applicant presents a complete nucleic acid sequence for human Hpr as Seq. ID No. 28. (p. 34, lines 16-17; Figure 11.) The gene encoding full length Hpr, or a truncation thereof, is only found in the primates: humans, gorillas, baboons, mandrills, chimpanzees, and sooty mangabeys. Lugli, EB et al, *Molecular & Biochemical Parasitology*, (2004); 138:9–20. Of these, only humans, baboons, and chimpanzees possess full length Hpr. *Id.* Further, these Hpr genes possess high sequence homology. *Id.* Previously, Hpr was detected in genes resulting in termination of transcription in chimpanzees. Smith et al, *Science*, (1995); 268:284-286. More recent studies by Lugli contradict those results and identify full length Hpr in chimpanzees as well. Thus, the total number of species of full-length primate Hpr genes is three. As the court in *Regents* stated: "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial

portion of the genus." *Regents of the Univ. of Calif. v. Eli Lilly & Co.*, 119 F.3d 1559 (Fed. Cir. 1997). This standard is precisely met by the instant specification. The description by nucleotide and amino acid sequence of the cDNA for Hpr recites "structural features common to the members of the genus" given the high homology between the Hpr genes in primates. *Id.* Further, the nucleotide and amino acid sequences described recite "features [that] constitute a substantial portion of the genus" of which there exist only three members. The court in *Regents* likened a similar satisfactory number of species to that which satisfies the enablement requirement. As such, description is readily met for a genus with a full one third of the total number of species expressly described, particularly given the high degree of sequence identity between members of the genus of primate Hpr genes.

Moreover, the recitation of the term Hpr is sufficient to describe the genus of primate Hpr genes with merely three species. This is similar to the generic term halogen found to be sufficient to describe the members of the chemical halogens. *Bigham v. Godtfredsen*, 857 F.2d 1415, 1417 (Fed. Cir. 1988) ("[t]he generic term halogen comprehends a limited number of species, and ordinarily constitutes a sufficient written description of the common halogen species.")

Claim 9 is canceled obviating any rejections as to a siRNA being a second therapeutic agent simultaneously delivered and consistent with the subject matter election.

In light of the above remarks, it is respectfully submitted that the instant specification provides support for claims 1-2, 7-8, 11, and 41 so as to convey to persons having ordinary skill in the art that Applicant had possession of the invention consistent with the requirements of 35 U.S.C. §112, first paragraph.

Remarks Directed to Rejection of Claims 1-2, 7-8, 11 and 41 under 35 U.S.C. §112, First Paragraph, Enablement

Withdrawal of the rejection of claims 1, 2, 7-8, 11 and 41 under 35 U.S.C. §112, first paragraph, for failing to comply with the enablement requirement is respectfully requested for at least the following reasons.

The basis for the maintenance of the outstanding enablement rejection is that the lysosomal trafficking detailed in Shimamura is considered not to have been established by that reference that predates the priority date of the instant application but rather merely cites lysosomal trafficking as a possibility. Reconsideration of the remarks made of reference in this regard is requested as well as rereading of the prior art reference Shimamura. Specifically, Applicant notes that Shimamura states "In this study, we present direct evidence for the lysosomal localization of TLF-1 and specifically Hpr." (Discussion, page 237).

It is respectfully submitted that a reading of Shimamura as a whole and specifically the teachings related to the above quotation therefrom affords a concrete teaching as to lysosomal targeting and as such, it is respectfully submitted that those pending claims will not lyse all species of *Trypanosoma*.

To bolster the remarks made of record with respect to introduction of lysosomes into a Trypanosome, Applicant provides as attachments previously cited references of Anzar et al., Kunisawa et al., Nakanishi et al., as well as U.S. Patent 4,356,167 (teaching liposomes once subjected to endocytosis stable for 48 hours per Example 6). Applicant apologizes for any inconvenience associated with the failure to provide such references earlier in the course of prosecution. In light of these teachings found in the prior art, it is respectfully submitted that actual introduction of liposomes into a trypanosome is well known in the art and as such the pending claims are enabled within the meaning of 35 U.S.C. §112.

In light of the above amendments and remarks, it is respectfully submitted that the instant specification provides teaching of claims 1-2, 4, 7-8, 11, and 41 so as to enable persons having ordinary skill in the art, or with which it is most nearly connected, to make and use the invention consistent with the requirements of 35 U.S.C. §112, first paragraph.

Remarks Directed to Rejection of
Claims 7-8, 11 and 41 under 35 U.S.C. §112, Second Paragraph

In response to rejections to claims 7-8 and 11, claims have been amended to recite with greater clarity that "the expression of said gene ... is upregulated by a promoter..." (emphasis added) as suggested on page 15 of the Paper 20070812.

In response to rejections to claim 41, claim 41 has been amended to provide greater clarity in that "primate Hpr" is a "primate Hpr protein."

In light of the above amendments and remarks, it is respectfully submitted that claims 7-8, 11 and 41 particularly point out and distinctly claim the subject matter which the Applicant regards as his invention consistent with the requirements of 35 U.S.C. §112, second paragraph.

Summary

With entry of this amendment, claims 1, 2, 4, 7, 8, 11 and 41 are submitted for reconsideration and allowance. Each of these claims is believed to be in allowable form and directed to patentable subject matter. Should the Examiner have any suggestions as to how to improve the form of any of the pending claims in light of the lack of prior art rejection she is respectfully requested to contact the undersigned attorney responsible for this application.

Dated: December 21, 2007

Respectfully submitted,

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